



Universiteit
Leiden
The Netherlands

Follow-up studies in prenatal medicine

Nagel, H.T.C.

Citation

Nagel, H. T. C. (2007, February 14). *Follow-up studies in prenatal medicine*.
Retrieved from <https://hdl.handle.net/1887/9762>

Version: Corrected Publisher's Version
License: [Licence agreement concerning inclusion of doctoral thesis in the Institutional Repository of the University of Leiden](#)
Downloaded from: <https://hdl.handle.net/1887/9762>

Note: To cite this publication please use the final published version (if applicable).

C H A P T E R 9

General Discussion

In the past decades, outpatient clinics have been instituted for the follow-up of extremely preterm born babies. Standard tests for assessment of neurodevelopment according to age are used. Trained staff is performing these tests. This follow-up is important for the evaluation of the therapies that have been used, for the guidance of the parents to the necessary support services for the child, and for update of the information that is presently used in counselling.

It seems clear that, with the introduction of new diagnostic procedures and therapies in fetal medicine, a structured follow-up should be standard of care in this field. Ideally, follow-up of infants should be performed at the right time, it should consist of the most relevant tests, and, in order to avoid bias, it should include all patients.

In the following, both the problems in determining the right child age for follow-up and suggestions for the optimal time will briefly be discussed. In addition, proposals will be given about the best test to be performed and how to enhance participation in follow-up after fetal diagnosis and therapy. Finally, the literature on perceived problems associated with incomplete follow-up will be summarized.

What is the optimum age for performing the follow-up? It is known that conditions such as diabetes or hypertension later in life may be associated with intrauterine growth retardation. Therefore, it may be necessary to wait until well into adulthood before obtaining a complete picture of all the consequences of prenatal diseases and interventions. However, because of constant development of new therapies and diagnostic tools, timely evaluation of these therapies by follow-up of mothers and infants is warranted. In addition, the later in life follow-up is performed, the more variables are involved that may influence the test results. In my opinion, two years of age is an appropriate age to test children after fetal interventions. The Bayley Scales of Infant Development (Second Edition-Dutch version: BSID-II-NL) can be used to test neurodevelopment in children aged two years.^{1,2} This test, for infants from one to 42 months of age, is often used in follow-up studies in the literature and consists of three separate scales (mental scale, motor scale, and behavioral rating). Mental and motor scale scores are converted to a mental developmental index (MDI) and a psychomotor developmental index (PDI). A second appropriate time to test is at the age of 5 to 6 years, because children are then attending school and can be tested for cognition, speech and language, behavior and social skills. At this age an almost complete picture can be obtained. An appropriate test at this age seems to be a questionnaire for the parents about school performance. Standardised and normalised instruments to detect neurological problems, developmental motor coordination disorders, learning and behavioral problems can also be used.

The aim is to obtain a 100% follow-up rate. This is more difficult when the time period that has elapsed since pregnancy is longer. Several factors may

contribute to a low follow-up rate. First, young families are at high risk to move and are therefore, easily lost to follow-up. Second, parents who have not come to terms with the disabilities of their child are likely to be lost to follow-up, because they are afraid for more medical interventions. In this thesis, we describe long-term outcome after several prenatal interventions trying to achieve as little loss to follow-up as possible. Strategies to achieve this included: counselling of parents during pregnancy that follow-up was planned, we were very persevering in trying to locate our patients, and very cautious in contacting them. In order to achieve this, the family physicians and referring physicians were contacted, to help us with the follow-up, telephone books were used, and city councils were contacted for addresses of the ones who moved. The strength of most of our studies is that there was only very few losses to follow-up. In general we observed that parents were very willing to contribute in the follow-up of their infants. Many couples were grateful for the care during the pregnancy and were happy to be able to do something in return for the medical team. To make follow-up easier in the future, we advise to inform parents during the pregnancy that standard follow-up will be done at a certain age of the child. It should be described in the patient information leaflet about the fetal intervention. When possible a home visit can be offered in case parents decline a hospital visit.

A problem in long-term follow-up is that the response rate decreases with the lapse of time between the original event and the follow-up assessment. It is not clear how the loss to follow-up influences the results of studies. McCormick *et al.* and Castro *et al.* suggest that those who are compliant with follow-up have more adverse outcome. Because children with a disability need continuing contact with health services and therefore are more easily contacted than healthy children.^{3,4} In contrast, a number of other studies have shown that loss to follow-up probably decreases the proportion of infants with adverse outcome because children who are lost to follow-up are at higher risk for developmental problems associated with a lower socio-economic background and a higher rate of developmental problems at an early age.^{5,9} Wolke *et al.* showed that non-response decreases the proportion of infants with adverse outcomes in assessed children because parents of disabled children are harder to persuade to cooperate in an assessment.⁵ Tin *et al.* found that the inclusion of children who were hard to follow-up raised the severe handicap rate by one third.¹⁰ In 1992, Jane Haliday reported on the importance of complete follow-up of spontaneous fetal loss after amniocentesis and chorionic villus sampling.¹¹ She found that women who are the most difficult to trace after amniocentesis or chorionic villus sampling are often those who have had an adverse pregnancy outcome. Both Wariyar *et al.* and Wolke *et al.* describe in their studies that parents who have not come to terms with their child's disability may tend to avoid situations where that disability is highlighted.^{5,8} Wariyar *et al.* states that it is difficult and expensive

to achieve a 100% follow-up.⁸ They suggest that trying to persuade those parents who seem to be reluctant for their children to be examined is a better way of reducing bias than tracking of families who are highly mobile. Hille *et al.* wrote that for many reasons 100% follow-up is not feasible.¹² This is not only true for perinatal studies but in all studies that evaluate late outcome. Follow-up reports should therefore include a drop-out analysis quantifying the extent by which those who did not participate at a later stage are more or less likely to have developmental problems and be more or less disadvantaged. In this way, comparison between different follow-up studies can be made more reliable.

In conclusion, outcome data, neonatal and long-term follow-up are extremely important in counselling families considering prenatal medicine. These families often have many questions concerning long-term outcome, because, as has been said in the introduction, the fetus is all future and no past. Centers involved in prenatal medicine have a responsibility to provide data on treated patients, including neonatal and long-term follow-up, and to publish the results of these follow-up studies in peer reviewed journals.

GENERAL DISCUSSION

References

1. Harris SR, Megens AM, Backman CL, Hayes VE. Stability of the Bayley II Scales of Infant Development in a sample of low-risk and high-risk infants. *Dev Med Child Neurol* 2005;47:820-3.
2. Voigt RG, Brown FR, III, Fraley JK, Llorente AM, Rozelle J, Turcich M, et al. Concurrent and predictive validity of the cognitive adaptive test/clinical linguistic and auditory milestone scale (CAT/CLAMS) and the Mental Developmental Index of the Bayley Scales of Infant Development. *Clin Pediatr (Phila)* 2003;42:427-32.
3. McCormick MC, Baker J, Brooks-Gunn J, Turner J, Workman-Daniels K, Peckham GJ. Cohort reconstruction: which infants can be restudied at school age? *Paediatr Perinat Epidemiol* 1991;5:410-22.
4. Castro L, Yolton K, Haberman B, Roberto N, Hansen NI, Ambalavanan N, Vohr BR, Donovan EF. Bias in reported neurodevelopmental outcomes among extremely low birth weight survivors. *Pediatrics* 2004;114:404-10.
5. Wolke D, Sohne B, Ohrt B, Riegel K. Follow-up of preterm children: important to document dropouts. *Lancet* 1995;345:447.
6. Stang A. Nonresponse research- an underdeveloped field in epidemiology. *Eur J of Epidemiol* 2003;18:929-31.
7. Hille ETM, Den Ouden AL, Bauer L, Van den Oudenrijn C, Brand R, Verloove-Vanhorick SP. Schoolperformance at nine years of age in very premature and very low birth weight infants: perinatal risk factors and predictors at five years of age. *J Pediatr* 1994;125:426-34.
8. Wariyar UK, Richmond S. Morbidity and preterm delivery: importance of 100% follow-up. *Lancet* 1989;1:387-8.
9. Hille ETM, Elbertse L, Bennebroek Gravenhorst J, Brand R, Verloove-Vanhorick SP. Nonresponse bias in a follow-up study of 19-year-old adolescents born as preterm infants. *Pediatrics* 2005;116:662-6.
10. Tin W, Fritz S, Wariyar U, Hey E. Outcome of very preterm birth: children reviewed with ease at 2 years differ from those followed up with difficulty. *Arch Dis Child Fetal Neonatal* 1998;79:F83-7.
11. Halliday JL, Lumley J, Sheffield LJ, Robinson HP, Renou P, Carlin JB. Importance of complete follow-up of spontaneous fetal loss after amniocentesis and chorion villus sampling. *Lancet* 1992;340:886-890.
12. Hille ETM, Den Ouden AL, Stuifbergen MC, Verrips GHW, Vogels AGC, Brand R, Bennebroek Gravenhorst J, Verloove-Vanhorick SP. Is attrition bias a problem in neonatal follow-up? *Early Human Dev* 2005;81:901-8.

REFERENCES

